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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/856,940	12/06/2001	Jamal Temsamani	19904-013 NALT	7834

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EXAMINER	
AEDER, SEAN E	
ART UNIT	**PAPER NUMBER**
1642	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	03/08/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	09/856,940	TEMSAMANI ET AL.	
	Examiner	Art Unit	
	Sean E. Aeder, Ph.D.	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 October 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-6* is/are pending in the application.

4a) Of the above claim(s) *2,3,5 and 6* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1 and 4* is/are rejected.

7)☒ Claim(s) *1 and 4* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *2/13/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Detailed Action

The Election filed 10/25/06 in response to the Office Action of 6/23/06 is acknowledged and has been entered. Applicant elected group II, as specifically drawn to peptides complying with the formula BXXBXXXXBBBXXXXXXB, with traverse.

The traversal is on the ground(s) that examination of all groups would not impose a serious burden on the examiner. This argument has been considered but is not found persuasive as such an argument does not apply when restriction is required under 35 USC 121 and 372, as in the instantly filed application. Thus, when the Office considers international applications as an International Searching Authority, as an International Preliminary Examining Authority, and during the national stage as a Designated or Elected Office under 35 U.S.C. 371, PCT Rule 13.1 and 13.2 will be followed when considering unity of invention of claims of different categories without regard to the practice in national applications filed under 35 U.S.C. 111. Further, it is noted that a search for the elected group, representing BXXBXXXXBBBXXXXXXB compounds, resulted in a 524 page search report. Therefore, even if a search burden was an issue, it is clear that searching the three additional classes of compounds of the unelected groups with the elected group would result in a serious search burden. For these reasons and the reasons stated in the Office Action of 6/23/06, the restriction requirement is deemed to be proper and is therefore made FINAL.

Claims 1-6 are pending.

Claims 2, 3, 5, and 6 are withdrawn from further consideration by the examiner under 37 CFR 1.142(b) as being drawn to a non-elected invention.

Claims 1 and 4 are currently under consideration.

Specification

The specification is objected to on page 4, 5, 9, 14, and 15 for improper disclosure of polypeptide sequences, as it fails to comply with the requirements of 37 CFR 1.821 through 1.825. This definition sets forth limits, in terms of numbers of amino acids and/or numbers of nucleotides, at or above which compliance with the sequence rules is required. Nucleotide and/or amino acid sequences as used in 37 CFR 1.821 through 1.825 are interpreted to mean an unbranched sequence of four or more amino acids or an unbranched sequence of ten or more nucleotides. (see MPEP 2422). Proper correction is required.

Claim Objections

Claim 1 is objected to for awkward recitation. Claim 1 recites: "...wherein formulas (II) and (III):...where the retro form of said formula (I), (II), (III) peptides composed of...". It is suspected Applicant intended claim 1 to recite: "...wherein formulas (II) and (III) **are further characterized in the following manner**:...where the retro form**s** of said formula (I), (II), **and** (III) peptides **are** composed of...". Proper correction is required.

Claim 4 is objected to for apparent typographical errors. Claim 4 recites: "...diaminopropionic acid, ornithine, and...3-pyridyalanine, [2-thienyl]alanine." It is suspected Applicant intended claim 4 to recite: "...diaminopropionic acid, **and** ornithine~~,~~; and...3-pyridyalanine, **and** [2-thienyl]alanine." Proper correction is required.

Claims 1 and 4 are objected to for reciting unelected inventions. The compositions comprising formula I and compositions comprising formula III are drawn to unelected groups 1 and 3, respectively.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1 and 4 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 and dependent claim 4 are rejected because claim 1 recites the limitation "the cancerous cells". There is insufficient antecedent basis for this limitation in the claim.

Claim 1 and dependent claim 4 are rejected because claim 1 recites the limitation "the identical or different B groups". There is insufficient antecedent basis for this

limitation in the claim. Although claim 1 recites polypeptides comprising formulas comprising "B", claim 1 does not recite what is meant by "the identical or different B groups".

Claim 1 and dependent claim 4 are rejected because claim 1 recites the limitation "the identical or different X groups". There is insufficient antecedent basis for this limitation in the claim. Although claim 1 recites polypeptides comprising formulas comprising "X", claim 1 does not recite what is meant by "the identical or different X groups".

Claim 1 and dependent claim 4 are rejected because claim 1 recites the limitation "the retro forms of said formula (I), (II), and (III) peptides". There is insufficient antecedent basis for this limitation in the claim. Although claim 1 recites formula (I), (II), and (III) peptides, claim 1 does not recite what is meant by " the retro forms" of said formula (I), (II), and (III) peptides.

Claim 1 and dependent claim 4 are rejected because claim 1 recites: "...said peptide complying with one of the following formulas...". It is unclear what is meant by "complying with". It is unclear whether Claim 1 is drawn to peptides consisting of a certain formula or peptides comprising a certain formula. This renders the claim indefinite because the term "complying" is not defined by the claim and one of ordinary

skill in the art would not be reasonably apprised of the scope of the invention. Given the above reasons, the metes and bounds of the claims cannot be determined.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1 and 4 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a pharmaceutical composition comprising at least one anti-cancer agent, characterized in that said anti-cancer agent is associated in the composition with at least one peptide capable of carrying said agent into cancerous cells, said peptide consisting of the following formula: BXXBXXXXBBBXXXXXXB, wherein B represents an amino acid residue in which the lateral chain comprises a basic group and X represents an aliphatic or aromatic amino acid residue, the specification does not reasonably provide enablement for making and using a pharmaceutical composition that treats and prevents cancer comprising at least one anti-cancer agent, characterized in that said anti-cancer agent is associated in the composition with at lest one peptide capable of carrying said agent into cancerous cells and preventing the occurrence of chemoresistance to said agent, said peptide complying with the following formula: BXXBXXXXBBBXXXXXXB, wherein B represents an amino acid residue in which the lateral chain comprises a basic group and X represents an aliphatic or aromatic amino acid residue. The specification does not

enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required are summarized in *Ex parte* Forman, 230 USPQ 546 (BPAI 1986). They include the nature of the invention, the state of the prior art, the relative skill of those in the art, the amount of direction or guidance disclosed in the specification, the presence or absence of working examples, the predictability or unpredictability of the art, the breadth of the claims, and the quantity of experimentation which would be required in order to practice the invention as claimed.

The instant claims are drawn to a pharmaceutical composition that treats and prevents cancer comprising at least one anti-cancer agent, characterized in that said anti-cancer agent is associated in the composition with at lest one peptide capable of carrying said agent into cancerous cells and preventing the occurrence of chemoresistance to said agent, said peptide complying with the following formula: BXXBXXXXBBBXXXXXXB, wherein B represents an amino acid residue in which the lateral chain comprises a basic group and X represents an aliphatic or aromatic amino acid residue. Recited features of the claimed composition is that it treats and prevents all cancers, prevents chemoresistance, and may comprise a peptide significantly larger than BXXBXXXXBBBXXXXXXB, wherein B represents an amino acid residue in which the lateral chain comprises a basic group and X represents an aliphatic or aromatic amino acid residue.

The specification teaches a pharmaceutical composition comprising at least one anti-cancer agent, characterized in that said anti-cancer agent is associated in the composition with at least one peptide capable of carrying said agent into cancerous cells, said peptide consisting of the following formula: BXXBXXXXBBBXXXXXXB, wherein B represents an amino acid residue in which the lateral chain comprises a basic group and X represents an aliphatic or aromatic amino acid residue (see Table I and Table II, in particular).

The specification does not provide any working examples using any composition from the broad class of compositions comprising an anti-cancer agent and a peptide complying with the following formula: BXXBXXXXBBBXXXXXXB, wherein B represents an amino acid residue in which the lateral chain comprises a basic group and X represents an aliphatic or aromatic amino acid residue to treat cancer, prevent cancer, and prevent the occurrence of chemoresistance to said agent. Further, while the specification provides an example of a composition comprising an anti-cancer agent and a polypeptide consisting of the following formula: BXXBXXXXBBBXXXXXXB, wherein B represents an amino acid residue in which the lateral chain comprises a basic group and X represents an aliphatic or aromatic amino acid residue that is able to deliver anti-cancer agents to cultured cells by carrying said agents into said cells, the specification does not demonstrate that peptides much larger than those consisting of BXXBXXXXBBBXXXXXXB, wherein B represents an amino acid residue in which the lateral chain comprises a basic group and X represents an aliphatic or aromatic amino acid residue, would predictably carry anti-cancer agents into cells. One of skill in the art

would recognize, due to their size, compositions comprising anti-cancer agents and very large polypeptides would not predictably be taken-in by a cell. Further, while it is noted that said peptides consisting of the following formula: BXXBXXXXBBBXXXXXXB, wherein B represents an amino acid residue in which the lateral chain comprises a basic group and X represents an aliphatic or aromatic amino acid residue are capble of carrying anti-cancer agents into chemoresistant cells, absent a showing to the contrary, one of skill in the art would recognize that said chemoresistant cells would remain chemoresistant to anti-cancer agents not linked to said peptides.

Further, therapeutic cancer treatments, in general, are unpredictable, as underscored by Gura (Science, 1997, 278:1041-1042.) who discusses the potential shortcoming of potential anti-cancer agents including extrapolating from in-vitro to in-vivo protocols, the problems of drug testing in knockout mice, and problems associated with cologenic assays. Indeed, since formal screening began in 1955, thousands of drugs have shown activity in either cell or animal models, but only 39 that are used exclusively for chemotherapy, as opposed to supportive care, have won approval from the FDA (page 1041 first column, in particular) wherein the fundamental problem in drug discovery for cancer is that the model systems are not predictive.

Further, in regards to a therapeutic that prevents cancer, reasonable guidance with respect to preventing any cancer relies on quantitative analysis from defined populations which have been successfully pre-screened and are predisposed to particular types of cancer. This type of data might be derived from widespread genetic analysis, cancer clusters, or family histories. The essential element towards the

validation of a preventive therapeutic is the ability to test the drug on subjects monitored in advance of clinical cancer and *link* those results with subsequent histological confirmation of the presence or absence of disease. This irrefutable link between antecedent drug and subsequent knowledge of the prevention of the disease is the essence of a valid preventive agent. Further, a preventive administration also must assume that the therapeutic will be safe and tolerable for anyone susceptible to the disease.

Further, those of ordinary skill in the art recognize that treatment in vivo is not predictive. The instant situation is analogous to that of *In re* Brana (34 U.S.P.Q. 2d 1436, 1440 (Fed. Cir. 1995)). A review of *In re Brana* reveals an application that claimed a chemical compound for treating a cancer, wherein the chemical compound was structurally similar to known compounds that have known in vivo use to treat tumors, and more importantly, Applicant provided in vivo data that the claimed compound could treat tumors in mice, hence it was ruled that the claimed compound was enabled for treating tumors. In the instant application, the claims are not drawn to compositions which have known in vivo ability to treat and prevent every cancer. Further, the instant specification provides no in vivo data, particularly demonstrating that the claimed composition would predictably treat and prevent every cancer in vivo. In view of *In re Brana*, Examiner asserts that successful use of in vivo mouse models of specific cancers enables compositions for specific therapeutic effects in humans and does not require human clinical testing; however, the instant application is claiming a composition that treats and prevents every cancer without providing any in vivo data,

hence the claimed invention is not enabled. All of this underscores the criticality of providing workable examples which are not disclosed in the specification, particularly in an unpredictable art, such as treating and preventing cancer.

One cannot extrapolate the teachings of the specification to the scope of the claims because the claims are broadly drawn to a pharmaceutical composition that treats and prevents cancer comprising at least one anti-cancer agent, characterized in that said anti-cancer agent is associated in the composition with at lest one peptide capable of carrying said agent into cancerous cells and preventing the occurrence of chemoresistance to said agent, said peptide complying with the following formula: BXXBXXXXBBBXXXXXXB, wherein B represents an amino acid residue in which the lateral chain comprises a basic group and X represents an aliphatic or aromatic amino acid residue, and Applicant has not enabled said composition because it has not been shown that compositions comprising anti-cancer agents and peptides consisting or comprising the following formula: BXXBXXXXBBBXXXXXXB, wherein B represents an amino acid residue in which the lateral chain comprises a basic group and X represents an aliphatic or aromatic amino acid residue, would predictably treat cancer, prevent cancer, and prevent chemoresistance to said agents.

In view of the teachings above and the lack of guidance, workable examples and or exemplification in the specification, it would require undue experimentation by one of skill in the art to determine with any predictability, that the method would function as claimed.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1 and 4 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 22-23 of copending Application No. 10/336312. Although the conflicting claims are not identical, they are not patentably distinct from each other because claims 23-24 of 10/336312 recite that the peptide of the pending claims are bound to "at least one active substance", whereas the pending claims recite that said peptide is bound to an anti-cancer agent. However, it is noted that the active substances disclosed in 10/336312 include anti-cancer agents (see page 22 of 10/336312, in particular).

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 1 and 4 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claim 28 of copending Application No. 10/490357. Although the conflicting claims are not identical, they are not patentably distinct from each other because claim 28 of 10/490357 recites a species of pending claims 1 and 4.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Summary

No claim is allowed.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sean E. Aeder, Ph.D. whose telephone number is 571-272-8787. The examiner can normally be reached on M-F: 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shanon Foley can be reached on 571-272-0898. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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